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Prospective Memory in Parkinson Disease During a Virtual Week: Effects of Both Prospective and Retrospective Demands

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Abstract

Objective—This study investigated the effect of Parkinson disease (PD) on event-based prospective memory tasks with varying demand on (1) the amount of strategic attentional monitoring required for intention retrieval (prospective component) and (2) the retrospective memory processes required to remember the contents of the intention or the entire constellation of prospective memory tasks.

Method—Twenty-four older adults with PD and 28 healthy older adults performed the computerized Virtual Week task, a multi-intention prospective memory paradigm that simulates everyday prospective memory tasks. The Virtual Week included *regular* (low retrospective memory demand) and *irregular* (high retrospective memory demand) prospective memory tasks with cues that were *focal* (low strategic monitoring demand) or *less focal* (high strategic monitoring demand) to the ongoing activity.

Results—For the regular prospective memory tasks, PD participants were impaired when the prospective memory cues were less focal. For the irregular prospective memory tasks, PD participants were impaired regardless of prospective memory cue type. PD participants also had impaired retrospective memory for irregular tasks, which was associated with worse prospective memory for these tasks during the Virtual Week.

Conclusions—When retrospective memory demands are minimized, prospective memory in PD can be supported by cues that reduce the executive control demands of intention retrieval. However, PD-related deficits in self-initiated encoding or planning processes have strong negative effects on the performance of prospective memory tasks with increased retrospective memory demand.

Keywords

Parkinson's disease; prospective memory; episodic memory; executive functioning; intention

Cognitive impairment is a well-recognized feature of Parkinson disease (PD) and is present in the earliest disease stages and in the absence of dementia (Aarsland, Bronnick, Larsen,

Tysnes, & Alves, 2009; Kudlicka, Clare, & Hindle, 2011). Although subtle, this impairment independently predicts reduced function and quality of life (Foster & Hershey, 2011; Klepac, Trkulja, Relja, & Babic, 2008). Cognitive impairment in PD without dementia involves, most prominently, deficits in executive control functions such as planning, working memory and cognitive flexibility (Cools, Barker, Sahakian, & Robbins, 2001; Gauntlett-Gilbert, Roberts, & Brown, 1999; Lewis, Slabosz, Robbins, Barker, & Owen, 2005; Owen et al., 1995). Individuals with PD also demonstrate declarative memory impairments, which are thought to stem from deficits in the executive control of encoding or retrieval processes rather than from deficits in retention (Bondi, Kaszniak, Bayles, & Vance, 1993; Bronnick, Alves, Aarsland, Tysnes, & Larsen, 2011; Buytenhuijs et al., 1994; Higginson et al., 2003; Taylor, Saint-Cyr, & Lang, 1990).

Prospective memory, or remembering to carry out previously formed intentions at the appropriate moment, is a complex cognitive construct (McDaniel & Einstein, 2007) that has received increasing attention in PD. Prospective memory tasks include such common everyday examples as remembering to take medication as prescribed, remembering to keep appointments, and remembering to return a library book on the due date. In event-based prospective memory, the appropriate moment is signaled by an external event. In terms of a single task, successful event-based prospective memory requires detecting the event and interpreting it as a cue for action (the *prospective component*) as well remembering the specific action to be performed (the *retrospective component*) (Einstein & McDaniel, 1996). On some accounts, the prospective component is thought to involve frontally mediated executive control processes that support monitoring for the event and initiating the intention (Burgess, Quayle, & Frith, 2001; Burgess & Shallice, 1997). Once the event is interpreted as a cue for action, retrieval processes similar to those involved in other associative memory tasks, such as recognition and cued-recall, support the retrospective component (Martin et al., 2007; Moscovitch, Schacter, & Tulving, 1994; Okuda et al., 1998; West & Krompinger, 2005). In everyday life, people often manage a number of intentions simultaneously (e.g., Marsh, Hicks, & Landau, 1998) so another source of retrospective memory demands in prospective memory is memory for all of the different tasks one has formulated for a given future period.

A number of studies have found that PD participants fail to carry out intentions despite remembering their contents upon later questioning (Foster, McDaniel, Repovs, & Hershey, 2009; Katai, Maruyama, Hashimoto, & Ikeda, 2003; Kliegel, Phillips, Lemke, & Kopp, 2005). This suggests that the retrospective memory processes involved in encoding and retention of intention contents are intact, while the executive processes underlying self-initiated intention retrieval or execution at the appropriate moment in the future are impaired (the prospective component). However, the opposite performance pattern has been reported, with PD participants demonstrating intact event-based intention retrieval but impaired recall of the intended action (i.e., they remembered *that* they were supposed to do something, but not *what* they were supposed to do; Costa, Peppe, Caltagirone, & Carlesimo, 2008).

The notion that particular features of prospective memory tasks can influence their executive control requirements has begun to guide more refined examinations of prospective memory in PD and can help to explain the above seemingly discrepant findings (see Kliegel, Altgassen, Hering, & Rose, 2011). In terms of the prospective component, the Multiprocess Theory (McDaniel & Einstein, 2000, 2007) proposes that intention retrieval can be supported by either controlled or automatic processes depending on, among other things, the nature of the prospective memory cue. A cue-related feature thought to strongly influence the executive control requirements of intention retrieval is *cue-focality*, or the degree to which critical features of the prospective memory cue are processed during the ongoing activity (see Einstein et al., 2005). Non-focal cues (those that are not fully processed as a

consequence of the ongoing activity in which an individual is engaged) require controlled attentional processes such as strategic monitoring for detection and intention retrieval; as such, performance on prospective memory tasks with non-focal cues has been linked to prefrontal cortical functioning (Burgess, Gonen-Yaacovi, & Volle, 2011). In contrast, focal cues are thought to elicit spontaneous intention retrieval when encountered in the context of the ongoing task, a process which is associated with the hippocampus (Gordon, Shelton, Bugg, McDaniel, & Head, 2011). Foster et al. (2009) manipulated cue-focality within an event-based prospective memory paradigm and found that while PD participants were impaired on tasks with non-focal cues, they were unimpaired on tasks with focal cues. Taken together, these studies suggest that the prospective component is not necessarily impaired by PD, but instead can be supported by cue-related features that facilitate automatic intention retrieval, thereby reducing executive control demands.

The idea that prospective memory task characteristics can alter demand on executive control can also be applied to more thoroughly investigate the contribution of retrospective memory processes to prospective remembering. The number of different intentions within a prospective memory paradigm (single vs. multiple; see Kliegel et al., 2011) or the complexity of their contents likely influence the amount of executive control required to effectively encode and retrieve the intentions and thus may affect memory for the entire prospective memory task (both the cue and action) or for the intention contents (the specific action associated with the cue), respectively. Although several studies have reported that retrospective problems do not interfere with prospective memory performance in PD, they used paradigms with a minimal number of simple intentions (e.g., “press a button when you see the word ‘cookie’”) (Foster et al., 2009; Katai et al., 2003; Pagni et al., 2011) or intentions that were simpler than those of the comparison group (Kliegel et al., 2005). Therefore, much existing work has not sufficiently challenged the retrospective memory processes involved in prospective memory.

Two studies that used more numerous or complex intentions did find PD-related impairments in the retrospective component (Costa, Peppe, Caltagirone et al., 2008; Raskin et al., 2010) and in retrospective memory for the entire task (Raskin et al., 2010). These apparent retrospective memory failures may have resulted from poor executive control during intention encoding and/or retrieval. For example, in the case of Costa, Peppe, Caltagirone et al. (2008), recalling the relatively complex intention of performing three unrelated actions (e.g., “ask the experimenter to turn off the computer, write your name on a paper, and replace the telephone receiver”) in response to a timer ring may have required a controlled memory search after spontaneous retrieval of the intention to do “something.” Deficits in controlled memory retrieval are a commonly-cited manifestation of frontostriatal circuitry dysfunction in PD (Troster & Fields, 1995). Paradigms with numerous or more complex intentions may also require higher-level encoding strategies or planning during the intention formation phase, and individuals with PD have been found to make limited use of such strategies (Buytenhuijs et al., 1994; Taylor et al., 1990). These findings indicate the need for a more focused examination of the effect of retrospective memory demand on prospective memory performance in PD.

Specifically, the common practice of minimizing retrospective memory demands may result in an underestimation of the role of controlled declarative memory processes in PD participants’ prospective memory performance. It may also result in a failure to capture the true demands of real-world prospective memory, which often involves multiple intentions with memory-demanding content. Given the prevalence of prospective memory tasks in daily life and their relevance for health and independence (e.g., Fortin, Godbout, & Braun, 2002; Woods et al., 2008), it is important to understand how PD-related prospective memory deficits manifest in real-world contexts. Unfortunately, experimental paradigms used thus

far may have low predictive validity for everyday prospective memory performance (e.g., Foster et al., 2009). The Virtual Week task (Rendell & Craik, 2000; Rendell & Henry, 2009) may help overcome this limitation, as it was designed to simulate the prospective memory requirements of daily life. The Virtual Week task takes the form of a board game that requires the coordination and execution of multiple intentions that resemble the types of prospective memory tasks people perform throughout their day (e.g., running errands, taking medications, making phone calls). Importantly, while possessing these naturalistic features, the Virtual Week is a controlled laboratory task, allowing for the manipulation of characteristics thought to influence the underlying cognitive requirements of various prospective memory tasks. Critical to the above discussion of prospective memory in PD, the Virtual Week includes event-based prospective memory tasks that vary in prospective-component and retrospective-memory demands (*cue-focality* and *regularity* [described below], respectively). Moreover, the Virtual Week has been found to be a more reliable index of prospective memory than traditional paradigms, as it includes a comparatively large number of prospective memory target trials (e.g., Rose, Rendell, McDaniel, Aberle, & Kliegel, 2010).

In this study, we employed the Virtual Week to conduct a more ecologically valid examination of prospective memory in PD. Specifically we aimed to replicate, in a more realistic context, the finding of Foster et al. (2009) that non-demented individuals with PD are preferentially impaired on event-based prospective memory tasks that require executive control for intention retrieval. We included event-based prospective memory tasks with *focal* and *less focal* cues, whereby focal cues served as an external trigger for intention retrieval and less focal cues required attentional strategies for detection and intention retrieval (details of how this factor was operationalized are in the description of the Virtual Week below).

A second objective was to investigate the effect of retrospective memory demand on prospective memory in PD, an issue that has received little attention to-date. To vary the demand on retrospective memory processes we included *regular* and *irregular* tasks. As outlined in previous reports of Virtual Week, retrospective memory demand is reduced for regular compared to irregular tasks (e.g., Rendell, Gray, Henry, & Tolan, 2007; Rendell & Henry, 2009; Rendell, Jensen, & Henry, 2007; Rose et al., 2010). In the current study, the retrospective memory demands of regular tasks were reduced in four ways. First, regular tasks received enhanced encoding relative to the irregular tasks because regular tasks were learned to criterion at the beginning of the game whereas irregular tasks were learned on the participants' own terms throughout the game. Second, the regular tasks were to be repeatedly performed across days and also within each day at the same moments in the game, whereas irregular tasks changed from day to day, both in terms of the intention and the specific cue to which that intention was linked. Third, because regular tasks were repeated across days and each irregular task was unique, there were fewer total cue-action associations to learn and remember for the regular tasks (4) compared to the irregular tasks (20) for the duration of the Virtual Week. Fourth, the content of the four regular tasks was of minimal complexity, as it only involved two relatively simple actions (taking antibiotics and using an asthma inhaler) that were related to one topic (dealing with a health problem). Irregular tasks, on the other hand, involved distinct actions and cues that were unrelated to each other. Thus, there were not only fewer total regular tasks compared to irregular tasks to learn and remember, but the content of the regular task intentions (i.e., the retrospective component) was less difficult.

Previous research has found that when retrospective memory demands are minimized, PD participants have a selective impairment for event-based prospective memory tasks with non-focal cues (Foster et al., 2009; Katai et al., 2003). Accordingly, we predicted that for the

regular tasks (those that presumably minimize the retrospective memory demand), PD participants would be impaired on those with less focal cues (challenging the prospective component McDaniel & Einstein, 2007) but unimpaired on those with focal cues relative to a comparison group of healthy older adults.

By contrast, for the *irregular* tasks (that we assume increase the retrospective memory demand), we anticipated that PD participants would be impaired regardless of whether cues were more or less focal. This expectation stems from our theoretical analysis presented above and from recent studies suggesting that PD participants had impaired prospective memory when demands on retrospective memory were relatively high (Costa, Peppe, Caltagirone et al., 2008; Raskin et al., 2010). It should be noted, though, that these studies used time-based tasks. Such tasks are analogous to less focal event-based tasks in that they require strategic monitoring of the environment (Einstein, McDaniel, Richardson, Guynn, & Cunfer, 1995), thereby placing high demands on the prospective component. Thus, these recent studies leave uncertain the degree to which challenges to retrospective memory versus the prospective component contribute to the observed PD-related prospective memory deficits. By examining prospective memory performance on a task with relatively high retrospective memory demands (the irregular prospective memory task) but lower prospective memory demands (a focal event-based irregular task), the current experiment allows a more penetrating evaluation of the role of retrospective memory processes in PD-related changes in prospective memory.

To provide support for our manipulation of retrospective memory demand, we assessed participants' retrospective memory for the various prospective memory tasks at the end of the Virtual Week (see *Retrospective memory test* below). We anticipated that for all participants, retrospective memory would be better (and almost perfect) for regular compared to irregular tasks. Due to the PD-related retrospective memory deficit hinted at in previous studies with more numerous or complex intentions (Costa, Peppe, Caltagirone et al., 2008; Raskin et al., 2010), we predicted that the PD group would have impaired retrospective memory for irregular tasks relative to the comparison group. Impaired retrospective memory for an intention likely interferes with its prospective execution. We predicted that this pattern would manifest on an individual level, with those with worse retrospective memory having worse prospective memory performance, as well as on a group level, with a PD-related deficit in irregular task retrospective memory contributing to a PD-related deficit in irregular task prospective memory performance.

Method

This study was approved by the Human Research Protection Office at Washington University School of Medicine (WUSM) and was completed in accordance with the Helsinki Declaration. All participants gave written informed consent before testing.

Participants

Study participants were 24 older adults with PD and 28 healthy older adults. PD participants were recruited from the WUSM Movement Disorders Center, and non-PD participants were volunteers from the community. All PD participants had been diagnosed with idiopathic PD by a movement disorders neurologist and were Hoehn and Yahr stage II (indicating relatively mild signs of disease; Hoehn & Yahr, 1967). Of the PD participants, 15 were receiving carbidopa-levodopa exclusively and 9 were receiving carbidopa-levodopa in conjunction with a dopamine agonist, COMT-inhibitor, or both ($n = 3$ each). Exclusionary criteria included possible dementia or global cognitive impairment (Mini-Mental State Examination (MMSE) score <27 ; Folstein, Folstein, & McHugh, 1975), treatment with anticholinergic medications, treatment with certain dopaminergic or benzodiazepine

medications known to interfere with cognitive functioning, history of neurosurgery or other neurological conditions (aside from PD for PD participants), history or current psychotic disorder, significant current psychiatric disorder, or any condition which would interfere with testing (e.g., non-English speaking, severe dyskinesias, inability to see testing materials, etc.).

Design

The type of prospective memory task was manipulated within-subjects, with the regularity of the task (regular, irregular) factorially combined with the cue type (focal, less focal) to yield 4 types of prospective memory tasks. As detailed (and justified) below, the focal cue prospective memory task was cued by an event card, whereas the less focal cue task was cued by a time square. In sum, the design constituted a 2 (Group: PD, non-PD) \times 2 (Regularity of the prospective memory task: regular, irregular) \times 2 (Cue type: focal, less focal) mixed factorial.

Procedure

Each participant underwent testing during one session that lasted about three hours. Because our goal was to conduct an investigation more representative of real-world prospective memory functioning, PD participants were tested while on their regular antiparkinsonian medications. Our previous study in a similar sample of PD participants found no effect of medication status on event-based prospective memory performance (Foster et al., 2009) (for different findings in relation to time-based prospective memory, see Costa, Peppe et al., 2008a, 2008b). Demographic information for both groups was obtained through interview. PD-related clinical characteristics, including on-medications motor dysfunction severity ratings within three months of the testing session (the United Parkinson's Disease Rating Scale Motor subscale, UPDRS; Fahn et al., 1987), were obtained from clinical chart review. All participants completed the Mill Hill Vocabulary Test (Raven, Court, & Raven, 1988) as a proxy for general intelligence and the 15-item Geriatric Depression Scale (GDS; Yesavage et al., 1982) to assess for depressive symptoms. Then they proceeded to cognitive testing, the details of which are described next.

Prospective memory test: Computerized Virtual Week—A recently computerized version of the Virtual Week board game was used for this study (Henry, Rendell, Kliegel, & Altgassen, 2007; Rendell & Henry, 2009; Rose et al., 2010). Participants performed this task on a desktop computer, using the mouse to interact with the software and move a game token around a “board” on the screen. Participants moved their token around the board by rolling a die (clicking on it in the middle of the screen) and then clicking on the corresponding square of the board. The consecutive hours of the day that people are typically awake (7:00am-10:00pm) were marked on the board, and each circuit of the board represented one day. As participants circuted the board, they progressed through the virtual time of day and encountered time-appropriate activities for which they were required to make decisions. Each time the token landed on or passed an event square (labeled “E”) participants were required to click on the “Event Card” button to reveal an event card that described a specific activity and three options relevant to the activity (e.g., “It’s breakfast. Do you have a) eggs, b) cereal, c) only coffee?”). Participants read each card, pretended to be engaged in that activity, and selected the preferred option. After the option was selected, the event card indicated a number to be rolled on the die in order to continue with the day (e.g., “You must roll an even number to continue.”). Rolling the die, circuiting the board, reading event cards, and making decisions about activity details served as the *ongoing activity* of this prospective memory paradigm.

Eight prospective memory tasks were embedded within each day: four regular tasks and four irregular tasks. Participants did not physically carry out the prospective memory tasks; rather they clicked on the “Perform Task” button when they felt it was the appropriate moment and selected the task from a list of possibilities (prospective memory tasks and distracters). The four *regular tasks* were repeated every day. These were “take antibiotics at breakfast and dinner” and “take asthma medication at 11 a.m. and 9 p.m.” Thus, upon reading the breakfast event card, participants were to remember to take their antibiotics by clicking on the “Perform Task” button and selecting “take antibiotics” from the list. Similarly, when the token landed on or passed the 9 p.m. square, participants were to remember to take their asthma medication by selecting it from the Perform Task list. All participants were required to learn the regular tasks to criterion (i.e., 100%) by completing a recall test three times with feedback provided following each test.

The four *irregular tasks* were different each day. Examples of irregular tasks were “drop off dry cleaning when you go shopping” and “phone the plumber at 4 p.m.” At the beginning of each day, participants were required to click on the “Start Card” button, which revealed a start card that described two of the irregular tasks for that day. The remaining two irregular tasks for each day were administered sometime during the day on event cards. For example, one event card read “You visit your nephew at school for lunch. He asks you to buy him some multi-colored pens when you go shopping today. In the meantime, do you have a) pizza, b) a sandwich, or c) a salad for lunch?” Then, later in the afternoon of that day, an event card informed participants that they were shopping. Upon reading this event card, participants were to remember to buy a multi-colored pen by selecting it from the Perform Task list.

As described above, participants were cued for the prospective memory tasks by either reading an event card that described a particular activity or by passing the token across a particular time square on the board¹. Rose et al. (2010) suggested that Virtual Week tasks cued by event cards and time squares are event-based tasks² that differ in their *cue-focality*, or degree to which the ongoing activity encourages processing of features of the cue emphasized during intention formation. Tasks to be performed on event cards were considered to have *focal* cues because reading and pretending to be engaged in the activity described on the card is central to the ongoing activity of the Virtual Week. In contrast, tasks to be performed at specified time squares were considered to have *less focal* cues because attending to the time square that one's token passed was not critical to the ongoing activity of the Virtual Week. Consistent with this hypothesis, Rose et al. (2010) showed that age differences were larger for tasks with less focal cues (i.e., the time-square cues) and that individual differences in working memory were correlated with performance on tasks with less focal cues, but not tasks with focal cues (the tasks associated with the event cards).

Participants completed five days with eight prospective memory tasks per day: four regular and four irregular. Within the regular and irregular tasks for each day, two of each had focal cues (event cards) and two had less focal cues (time squares). This yielded a total of 40 prospective memory tasks across four task types: 10 regular focal, 10 regular less focal, 10 irregular focal and 10 irregular less focal. For regular and irregular less focal tasks, responses were considered correct if they occurred within one virtual hour of the target time.

¹We did not include the time-check tasks that can be a part of the Virtual Week (i.e., check lung capacity at 2min 15sec and 4min 30sec after the start of each day) in this study because our purpose was to investigate event-based prospective memory in PD. A number of previous studies with Virtual Week as the primary measure have excluded these tasks (e.g., Ozgis, Rendell, & Henry, 2009; Paraskevaides et al., 2010; Thompson, Henry, Rendell, Withall, & Brodaty, 2010).

²Because the times were marked on the squares of the board, the “time-based” tasks of the present version of the Virtual Week did not require monitoring a clock or the passage of real time as in true time-based prospective memory tasks. Instead, moving one's token past a time square can be conceptualized as an event, as it involved encountering an external cue.

For regular focal tasks, responses were considered correct if they occurred between the event cards immediately preceding and following the target event card, a period which roughly corresponds to the on-time criteria set for the less focal tasks. Therefore, in the regular focal condition and in both of the less focal conditions slightly early responses were considered correct because the breakfast and dinner event cards and the time squares could reasonably be anticipated within the context of the game. In contrast, in the irregular focal condition, only responses occurring at the target event card or before the next event card were considered correct (because participants did not know when the irregular events would occur and thus presumably could not have anticipated the target event card for the irregular focal task). Additional performance errors including number of perform task list cancellations (opening the list but not selecting a task), number of distracters selected, and “double doses” were also recorded. A double dose indicates the repeated selection of a specific prospective memory task. In some cases, a task is completed early and then repeated at the correct time (second correct); thus, the repeat appears to be a correction.

Participants received detailed verbal instructions on the Virtual Week and were guided through one trial day with four irregular tasks (two focal, two less focal) by the experimenter. During this time they were free to ask questions, and the experimenter ensured they were comfortable with the computer and the task. After the trial day but before beginning the test days, participants were introduced to the regular tasks and were required to learn them to criterion (i.e., 100%) by completing a recall test three times, with feedback provided following each test. The participants were instructed to perform the same four regular tasks each test day and were reminded that, similar to the trial day, they would be given four different irregular tasks to perform each test day that would not be repeated (two would be given at the beginning of each day and two would be given during each day). Participants then completed the five test days (Monday-Friday) of the Virtual Week on their own.

Retrospective memory test—Immediately following the Virtual Week, participants completed a recognition test to assess their retrospective memory for the various prospective memory tasks of the Virtual Week. The test involved matching each intended action with its cue. Participants were presented with a list of the actions (e.g., take antibiotics, phone the plumber) on the left side of a sheet of paper and a list of the cues (e.g., dinner, 4:00 pm) on the right. They were to draw lines connecting the appropriate pairs and were encouraged to connect every action with a cue even if they were unsure. There were 24 items on the test: 4 regular tasks (2 focal, 2 less focal) and 20 irregular tasks (10 focal, 10 less focal). Proportion correct was calculated for each task type (regular focal, regular less focal, irregular focal, irregular less focal).

Results

All statistical tests were 2-tailed. An alpha level of $p < 0.05$ was considered significant, and effect sizes were estimated using partial eta squared (η^2).

Participant Characteristics

Demographic and clinical characteristics of the participants are presented in Table 1. Due to experimenter error (score sheets misplaced), a portion of the non-PD groups' GDS and MMSE data are missing; however, no non-PD participants scored < 27 on the MMSE or above the GDS screening cutoff for depressive disorder. The sample was 54% female and 96% Caucasian. There were no significant group effects with regard to age, education, MMSE score, or Mill Hill score ($ps > 0.19$). The PD group reported significantly more depressive symptoms than the control group as measured by the GDS, $t = -2.93$, $p = 0.006$;

however, only one PD participant scored above the GDS screening cutoff for depressive disorder (cutoff = 5, participant's score = 9). Depression was not associated with prospective memory performance within the PD group ($r_s < 0.15$, $p_s > 0.47$).

Virtual Week

Reliability—The reliability coefficients (Cronbach's α) for the four prospective memory task types of the Virtual Week are presented in Table 2. The data for the PD participants (see top row in Table 2) indicate that the computerized Virtual Week is a reliable measure of prospective memory in PD.

Prospective memory—Proportions of correct prospective memory responses are presented in Figure 1. These data were submitted to a mixed analysis of variance (ANOVA) with group (PD, non-PD) as the between-subjects factor and regularity (regular, irregular) and cue type (focal, less focal) as the within-subjects factors. In general, PD participants were disadvantaged in prospective memory relative to the non-PD participants, $F(1, 50) = 8.33$, $p = 0.006$, $\eta^2 = 0.14$. In addition prospective memory performance was generally higher with regular than with irregular cues, $F(1, 50) = 226.12$, $p < 0.001$, $\eta^2 = 0.82$, and higher with focal than with less focal cues, $F(1, 50) = 15.20$, $p < 0.001$, $\eta^2 = 0.23$. These main effects were qualified by a marginally significant three-way interaction, $F(1, 50) = 3.81$, $p = 0.06$, $\eta^2 = 0.07$ (see Figure 1). To help interpret this interaction and to evaluate the predictions outlined in the introduction, separate two-way ANOVAs for regular and irregular tasks (with group and cue type as variables) were performed. For regular tasks, there was a significant two-way interaction between group and cue type, $F(1, 50) = 3.92$, $p = 0.05$, $\eta^2 = 0.07$. A test of simple effects showed that PD participants performed worse than non-PD participants on less focal tasks, $F(1, 50) = 6.46$, $p = 0.01$, $\eta^2 = 0.11$, but not focal tasks, $F(1, 50) = 0.87$, $p = 0.36$, $\eta^2 = 0.02$. For irregular tasks, PD participants performed worse than non-PD participants, $F(1, 50) = 9.18$, $p = 0.004$, $\eta^2 = 0.16$, and this effect did not interact with cue type, $F = 0.95$. Also, all participants performed worse on less focal compared to focal tasks, $F(1, 50) = 26.38$, $p < 0.001$, $\eta^2 = 0.35$. To summarize, as anticipated PD participants were impaired on regular less focal, irregular focal and irregular less focal prospective memory tasks compared to non-PD participants.

We performed two additional analyses to (a) determine the effect of repeatedly performing the same prospective memory task (regular tasks) across the days of the Virtual week and (b) determine whether enhanced encoding per se contributed to the advantage of regular tasks relative to irregular tasks. Proportions of correct prospective memory responses for regular tasks (collapsed across focal and less focal cues) on each day of the Virtual Week were submitted to a 2 (group) X 5 (day of the week) ANOVA. Regular task prospective memory performance improved over the course of the week in both groups, $F(4, 47) = 3.70$, $p = 0.006$, $\eta^2 = 0.07$. This effect did not interact with group, $F(4, 47) = 0.63$, $p = 0.64$, $\eta^2 = 0.01$, indicating that PD and non-PD participants benefitted similarly from repetition.

To isolate the potential benefit of enhanced encoding associated with the regular prospective memory tasks, we analyzed the proportions of correct prospective memory responses for regular and irregular tasks on the first day of the Virtual Week (Monday). The 2 (group) X 2 (regularity) ANOVA indicated that prospective memory was better for regular tasks ($M = 0.81$, $SD = 0.24$) than for irregular tasks ($M = 0.43$, $SD = 0.29$) on the first day of the game, $F(1, 50) = 83.06$, $p < 0.001$, $\eta^2 = 0.62$. PD participants had worse prospective memory performance than non-PD participants on the first day of the game, $F(1, 50) = 8.15$, $p = 0.006$, $\eta^2 = 0.14$, but this effect did not interact with regularity, $F(1, 50) = 2.25$, $p = 0.14$, $\eta^2 = 0.04$. Thus, both the enhanced encoding that regular tasks received before beginning the

test and the repetition of these regular tasks contributed to the enhanced prospective memory performance.

Retrospective memory—Proportions of correct retrospective memory responses for each group and task type are presented in Table 3. Due to the limited variance in retrospective memory for regular tasks (only one non-PD and two PD participants had less than 100% accuracy on these items), we did not analyze these data further. Irregular task retrospective memory scores were submitted to a mixed ANOVA with group (PD, non-PD) as the between-subjects factor and cue type (focal, less focal) as the within-subjects factor. In line with the expectations outlined in the introduction, PD participants had worse retrospective memory for irregular tasks than non-PD participants, $F(1, 50) = 5.42, p = 0.02, \eta^2 = 0.10$. In both groups, memory was better for irregular tasks with focal cues compared to those with less focal cues, $F(1, 50) = 48.91, p < 0.001, \eta^2 = 0.49$.

Association of prospective and retrospective memory for the irregular tasks—Retrospective memory for irregular tasks was strongly correlated with prospective memory for irregular tasks for both groups (PD: $r = 0.78, p < 0.001$; non-PD: $r = 0.76, p < 0.001$). We conducted a pair of stepwise linear regression analyses predicting prospective memory for irregular tasks with focal or less focal cues to determine if retrospective memory completely or partially mediated the effect of PD. For irregular focal tasks, retrospective memory accounted for 27% of the variance, $F(1, 50) = 18.36, p < 0.001$, and group added an additional 6% of the variance, $F\Delta(1, 49) = 4.26, p = 0.04$. For irregular less focal tasks, retrospective memory accounted for 66% of the variance, $F(1, 50) = 97.60, p < .001$, but group did not add a significant amount of variance ($p = 0.72$). Thus, retrospective memory partially mediated the effect of PD on prospective memory for irregular focal tasks and completely mediated the effect of PD on prospective memory for irregular less focal tasks.

Prospective memory conditionalized on retrospective memory for the irregular tasks—Proportions of correct prospective memory responses for only those irregular tasks for which retrospective memory was accurate are presented in Table 4. These data were submitted to a mixed ANOVA with group (PD, non-PD) as the between-subjects factor and cue type (focal, less focal) as the within-subjects factor. There were no significant effects of group, $F(1, 50) = 2.90, p = 0.095, \eta^2 = 0.06$, or cue type, $F(1, 50) = 0.09, p = 0.769, \eta^2 < 0.01$, nor was there an interaction effect, $F(1, 50) = 2.54, p = 0.117, \eta^2 = 0.05$. Therefore, when the content of the irregular prospective memory tasks were accurately remembered by those with PD on the retrospective memory post-test, their prospective memory was similar to non-PD participants.

Additional performance errors on the Virtual Week—There were no significant group effects in terms of the additional errors recorded (all $ps > 0.17$; Table 5). Double doses were notably low in both groups (PD $M = 2.17, SD = 1.76$; non-PD $M = 2.36, SD = 2.8$) relative to the total number of prospective memory tasks (40).

Discussion

Our purpose was to investigate the cognitive mechanisms underlying complex event-based prospective memory performance in PD. We aimed to determine whether the previously found preferential impairment on tasks requiring executive control for intention retrieval (i.e., less focal prospective memory tasks) could be replicated in a more realistic context. We also addressed the effect of retrospective memory demand on prospective memory performance in PD, an issue that has been largely disregarded in studies to-date. To this end, we used the Virtual Week task, a multi-intention paradigm that mimics daily life, and

compared the effects of cue-focality and regularity on the prospective memory performance of non-demented individuals with PD and healthy comparison participants. As hypothesized, we found that PD participants were impaired on prospective memory tasks that required attentional strategies for intention retrieval (i.e., tasks with less focal cues) regardless of retrospective memory demand. However, when retrospective memory demand was higher (i.e., irregular tasks), PD participants were also impaired on tasks thought to rely on relatively automatic retrieval processes (i.e., tasks with focal cues).

Our data are consistent with previous research in that, at least when retrospective demand is minimized (i.e., the regular tasks), non-demented individuals with PD demonstrate a preferential impairment for less focal event-based prospective memory tasks—tasks that require attentional control strategies for intention retrieval (Foster et al., 2009; Katai et al., 2003). Focal and less focal regular tasks were encoded in the same manner and elicited nearly perfect post-test recognition, so it is unlikely that the impairment for less focal regular tasks was a result of deficits in intention formation or retention. In addition, both of these conditions required inhibition of the ongoing activity and switching to actions required to perform the prospective memory task after intention retrieval, so deficits in the intention execution phase also cannot account for the impairment on less focal regular tasks.

The primary difference between focal and less focal regular tasks was the degree to which the ongoing activity encouraged processing of the prospective memory cue³. Tasks cued by event cards are considered to be more focal because they are processed more fully during the ongoing activity of Virtual Week, which involves reading event cards and pretending to be engaged in the events. Tasks cued by passing one's token over a particular square on the board are considered to be less focal because this action is peripheral to the ongoing activity in the game (Rose et al., 2010). Whereas focal cues can elicit automatic intention retrieval when encountered within the context of the ongoing activity, less focal cues require additional attentional control processes to be recognized (Einstein et al., 2005; McDaniel & Einstein, 2000). This notion has been supported in PD, as performance on prospective memory tasks with less focal, but not focal, cues is associated with ongoing activity response time costs and performance on executive control tasks (Costa, Peppe, Caltagirone et al., 2008; Foster et al., 2009). The PD-related deficit for less focal tasks could be due to impaired active maintenance of the intention in working memory (Burgess et al., 2001), impaired monitoring of the environment for the cue while also engaging in the ongoing task (Reynolds, West, & Braver, 2009), or impaired internally-driven shifting of attention from stimuli relevant to the ongoing activity to a less relevant or salient cue (Cools, Rogers, Barker, & Robbins, 2010). Our study was not designed to determine the potential differential contributions of these executive control processes. Regardless, our results indicate that intention retrieval in PD is facilitated by cues which reduce demand on these processes.

When retrospective memory processes were challenged (i.e., the irregular tasks), the PD group had impaired prospective memory for both focal and less focal tasks. This impairment

³Although there was no effect of cue-focality on regular task performance in the non-PD group, which is somewhat at odds with what would be expected based on the Multiprocess Theory (McDaniel & Einstein, 2000, 2007), it should be noted that the conceptualization of cue-focality in the present version of the Virtual Week task was not as strictly controlled as in other prospective memory paradigms. The exact event-card (focal) cues were not presented during task encoding, and it is possible that these cues were not fully processed when encountered later due to the other demands of the ongoing activity (selecting activity options). In addition, although attending to the times marked on the squares was not critical to the ongoing activity of the Virtual Week, participants may have nonetheless done it while moving their tokens or as a general way of keeping track of the progression of the virtual day. Cue-focality is a matter of degree in the current study rather than an absolute distinction, which is why these tasks were termed “less focal” instead of “non-focal”. This may also help to explain why the group difference was larger (although not significantly so) for Irregular Focal tasks than for Irregular Less Focal tasks, although it is important to note that both groups had the most difficulty with the Irregular Less Focal tasks.

was largely accounted for by deficient retrospective memory for the irregular tasks as measured by the post-test recognition task. The irregular condition of Virtual Week is thought to impose greater demands on retrospective memory processes than the regular condition because it involves twenty different and unrelated cue-action associations (compared to just four related and repeated cue-action associations in the regular condition) which do not receive enhanced encoding (as do tasks in the regular condition) (Rendell & Henry, 2009). The nearly perfect retrospective memory for regular tasks but significantly reduced retrospective memory for irregular tasks among all participants in the present study supports this claim. The PD group had worse retrospective memory for irregular tasks than the non-PD group, and this was strongly associated with worse prospective memory for irregular tasks during Virtual Week. Furthermore, when only those tasks with accurate retrospective memory were considered (the conditional analyses), the PD-related prospective memory deficit for irregular tasks went away. These findings are consistent with those of Raskin et al. (2010), who found a PD-related post-test recognition deficit for irregular intentions and significant associations between retrospective and prospective memory performance within PD. Previous studies have also found increased task substitution errors (indicating mis-remembering of intention contents; Raskin et al., 2010) and impaired recall of the intended action after intention retrieval in PD (Costa, Peppe, Caltagirone et al., 2008). Taken together, these results suggest that the retrospective memory processes involved in prospective memory can be disrupted by PD.

It should be noted that the retrospective memory post-test in the current study is only a general indicator of retrospective memory for the prospective memory tasks because it was not administered until the end of the five virtual days. Factors such as interference with new tasks that were to-be-remembered or the length of the retention interval (up to approximately 40 minutes for Monday's tasks) could have affected performance on the retrospective memory post-test without necessarily being indicative of retrospective memory load-related forgetting during the game. This may account for the partial mediation of irregular task prospective memory performance by irregular task retrospective memory. In addition, the retrospective memory post-test does not allow determination of the potential source of impaired task performance during the course of the game. For example, failure on the post-test could indicate that the participant forgot only the cue-action association (which means s/he could have retrieved the intention to do *something* upon encountering the cue during the game but could not retrieve the contents of the intention, i.e., a retrospective component failure), or it could indicate that the participant forgot the entire task (and thus did not even retrieve the intention to act during the game). Since these data were collected, the Virtual Week has been upgraded to include a retrospective component assessment at the end of each virtual day. Meanwhile, a more complete picture may be provided by the additional performance errors on the Virtual Week. If the retrospective memory problem is an associative one, it should be characterized by Perform Task list cancellations and selection of distracters from the Perform Task list. There were no group differences in these measures, and Distracter selection was a rare error in both groups, suggesting that participants were forgetting the entire prospective memory task.

Given that non-demented individuals with PD consistently demonstrate intact memory retention (Bronnick et al., 2011) and that the recognition format of the Perform Task list and of the retrospective memory post-test placed few demands on controlled retrieval processes, it is unlikely that the PD-related retrospective memory deficit for irregular tasks was related to impaired storage or retrieval of intention contents. Instead, we propose that it was largely a function of poor executive control of encoding during the intention formation phase. Although we did not directly assess the differential effects of encoding and retrieval, previous research on memory dysfunction in PD supports this explanation. Participants were left to encode irregular tasks on their own throughout the duration of the game, so optimal

encoding of these tasks required a high degree of self-initiation. In contrast, the experimenter guided regular task encoding at the beginning of the game by supplementing computer administration with verbal explanation and requiring participants to recall the tasks while providing corrective feedback until the tasks were learned to criterion. In this way, full encoding of the regular tasks was externally-enforced. The self-initiation of good encoding strategies is a frontally-mediated executive process (Buckner, Logan, Donaldson, & Wheeler, 2000). Studies of retrospective memory have shown that individuals with PD fail to self-initiate effective encoding strategies, and this contributes to deficient recall (Bronnick et al., 2011; Buytenhuijs et al., 1994; Taylor et al., 1990). However, when provided with explicit encoding strategies, PD patients can use them to essentially normalize their performance (Knoke, Taylor, & Saint-Cyr, 1998; Scholz & Sastry, 1985).

In the present study, it is likely that without explicit instruction the PD participants did not optimally encode the irregular intentions, which resulted in the prospective memory deficit. This explanation is consistent with the findings of two studies of prospective memory in PD by Kliegel and colleagues. In a paradigm which involved self-directed formation of a complex delayed intention, individuals with PD formed less elaborate plans for accomplishing the intention relative to a control group and subsequently were less likely to retrieve and initiate the intention when the target event occurred (Kliegel et al., 2005). In a follow-up study, Altgassen, et al. (2007) more closely examined the intention formation phase by using instructions that differentially emphasized the importance of the prospective memory task relative to the ongoing activity in two versions of a challenging event-based paradigm. PD participants had impaired prospective memory when the ongoing activity was emphasized, but they performed just as well as controls when the prospective memory task was emphasized. Therefore, it appears that when challenging intentions are involved, individuals with PD do not spontaneously implement higher-order encoding or planning strategies necessary to support later remembering, but this process can be facilitated by externally-guided direction of attention to the intention during encoding. Working memory capacity was strongly associated with the intention formation effects in both of the studies just described (Kliegel et al.; Altgassen et al.), which is consistent with the idea that deficits in executive control underlie this retrospective memory problem in PD.

Still at issue is why retrospective memory for the less focal irregular tasks was poorer than for the focal irregular tasks. In this experiment, retrospective memory for the less focal irregular tasks may have been especially compromised by the arbitrary relation between the cues and intended actions. For instance, the less focal cues were time squares (virtual times) that did not inherently relate to the intention (4 PM—phone the plumber). By contrast, focal cues were events (go shopping) that could be meaningful linked to the intended action (pick up dry cleaning), and may have even reflected the participants' everyday experiences. Certainly, the relatively arbitrary cue-action association for the less focal irregular tasks could have compromised encoding. However, it is theoretically plausible that the poorer retrospective memory by both PD and non-PD groups for less focal compared to focal tasks may reflect difficulty retrieving less well-related cue-action associations. Greater retrieval difficulty for these associations (in the less focal irregular tasks) could have also been the reason that retrospective memory for the cue-action pairings entirely mediated the PD-related prospective memory deficit for the less focal irregular tasks (a finding that was not expected a priori). These findings leave open the possibility that a memory retrieval deficit, rather than or in addition to an encoding deficit, impairs the retrospective memory involved in prospective memory in PD. We could not parse the effects of these component processes in the current experiment, but it is clear that the retrospective memory demands of prospective remembering warrant further investigation in this population.

Our findings and interpretation are in line with the notion that PD produces a fundamental deficit in the allocation of attentional resources without explicit external cues (Brown & Marsden, 1988; Cools, van den Bercken, Horstink, van Spaendonck, & Berger, 1984). PD-related performance decrements on tasks that require the generation and use of internal organizational strategies to optimize goal-directed behavior have been found across a variety of domains (Pillon, Boller, Levy, & Dubois, 2001). This deficit is thought to arise from frontostriatal circuitry dysfunction (Taylor, Saint-Cyr, & Lang, 1986), particularly the circuit encompassing the dorsal portion of the caudate nucleus and its projections to the dorsolateral prefrontal cortex (Alexander, DeLong, & Strick, 1986; Owen, 2004). Dorsolateral prefrontal cortical activity has been linked to the maintenance of a delayed intention in healthy participants (Burgess et al., 2001), particularly in tasks with high working memory load (Basso, Ferrari, & Palladino, 2010; Reynolds et al., 2009). However, the region most consistently associated with prospective memory in neuroimaging studies is the anterior prefrontal cortex (Burgess et al., 2011; Reynolds et al., 2009), and the specific effect of PD on this region is not well-studied. Further research is required to delineate the neural mechanisms underlying the effect of PD on prospective memory.

In summary, our data highlight the negative effect of executive control requirements on prospective memory performance in PD using a reliable and complex multi-intention paradigm. In addition to affecting the prospective component (i.e., self-initiated intention retrieval), deficits in strategic attentional processing among individuals with PD can also interfere with retrospective memory processes critical to prospective memory performance. While intention retrieval may be supported by features that facilitate automatic processing of prospective memory cues, deficits in self-generated encoding strategies or planning at intention formation can preclude this benefit. This implies that the presence of multiple intentions with complex content may call for the additional provision of explicit intention formation strategies (e.g., implementation intentions; Gollwitzer, 1996). Prospective memory is considered essential for everyday function and is associated with important clinical outcomes in other neurological populations, including independence in activities of daily living (Fortin, Godbout, & Braun, 2003; Woods et al., 2008) and caregiver burden (Smith, Della Sala, Logie, & Maylor, 2000). A better understanding of what causes prospective memory impairment in PD will guide the development of targeted interventions to improve it. Because the ultimate goal is to improve individuals' prospective memory in everyday life, it is important that we begin conducting investigations that capture the complexity of real-world prospective memory tasks. This includes using assessments that are more representative of people's daily lives and acknowledging the fact that many real-world prospective memory tasks challenge retrospective memory. Tasks like the Virtual Week, which have better face validity and psychometric properties compared to previous paradigms used to investigate prospective memory in PD (e.g., Foster et al., 2009; Raskin et al., 2010), may provide better insight into the factors that influence real-world prospective memory in PD and perhaps a clearer path to intervention.

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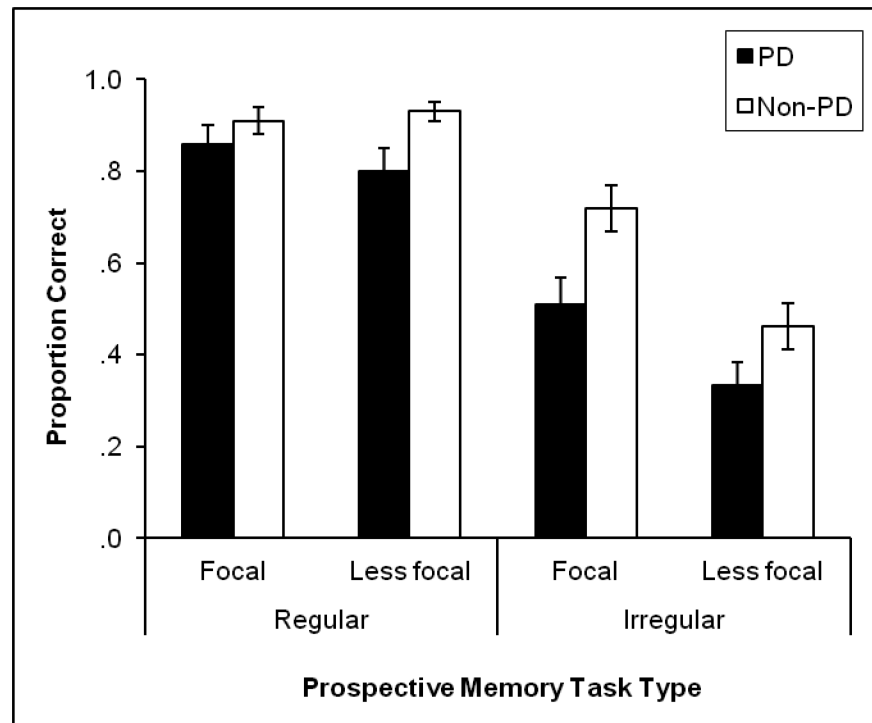


Figure 1. Prospective memory performance: Mean proportion of correct responses on prospective memory tasks in the Virtual Week as a function of clinical group, cue type and task regularity. Error bars depict standard error of the mean.

Table 1

Characteristics of the participants, N=52.

Variable	PD	non-PD
n	24	28
Age (years)	67.0 (5.9)	69.2 (5.9)
Education (years) ^a	15.3 (2.8)	16.5 (2.8)
GDS ^b	2.3 (1.8)	0.7 (0.9)*
MMSE ^c	29.4 (0.7)	29.1 (0.9)
Mill Hill Vocabulary	14.7 (1.7)	15.0 (2.4)
Disease duration (years)	5.7 (4.3)	--
UPDRS Motor	19.5 (9.0)	--
LEDD (mg)	1039 (579)	--

Values are shown as mean (standard deviation) or number of participants. Variables with missing data are indicated with superscript letters as follows:

GDS = 15-item Geriatric Depression Scale; MMSE = Mini-Mental State Examination; UPDRS Motor = Unified Parkinson Disease Rating Scale, Motor subscale; LEDD = Levodopa equivalent daily dose.

^a control n=26

^b control n=13

^c control n=16.

* $p < 0.05$

Table 2

Reliability of Virtual Week: Cronbach's alpha assessing internal consistency.

	Regular focal	Regular less focal	Irregular focal	Irregular less focal	Overall
Number of items	10	10	10	10	40
PD	0.79	0.79	0.73	0.63	0.89
non-PD	0.74	0.75	0.74	0.70	0.81

Table 3

Retrospective memory performance: Proportion of correct retrospective memory responses for the prospective memory tasks of the Virtual Week.

Type of task	PD	non-PD
Regular focal ^a	0.96 (0.14)	0.98 (0.09)
Regular less focal ^a	0.96 (0.14)	0.98 (0.09)
Irregular focal ^b	0.55 (0.21)	0.68 (0.21) *
Irregular less focal ^b	0.37 (0.22)	0.50 (0.22) *

Values are shown as mean (standard deviation).

^aOut of 2 items

^bOut of 10 items

* PD worse than non-PD, $p < 0.05$

Table 4

Proportion of correct prospective memory responses conditionalized on correct retrospective memory responses for irregular tasks.

Type of task	PD	non-PD
Focal	0.56 (0.32)	0.75 (0.24)
Less Focal	0.66 (0.27)	0.68 (0.30)

The formula for this index is $\#PM_{correct}|RM_{correct}/(\#PM_{correct}|RM_{correct} + \#PM_{incorrect}|RM_{correct})$. Values are shown as mean (standard deviation).

Table 5

Number of additional errors on the Virtual Week.

	PD	non-PD
Perform Task List cancellations	8.92 (10.48)	5.36 (5.18)
Distracters selected	0.67 (1.24)	0.29 (0.71)
Double doses ^a		
2 nd correct	1.38 (1.24)	1.82 (2.13)
All other	0.79 (1.10)	0.54 (1.07)

Values shown as mean (standard deviation).

^a Out of 40 tasks